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Title: Planned and unplanned pregnancies in breast cancer survivors

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Keywords: unplanned pregnancies, breast cancer survivors, contraception, pregnancy rate

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Abstract: Abstract
Background
Nearly 20% of women presenting with breast cancer in the UK are of reproductive age. The aim of our study was to assess fertility outcome in relation to intent to conceive in patients who had completed breast cancer treatment.
Methods
Between July 2011 and December 2013, women, aged less than 43 years at the time of diagnosis, were asked during their follow-up in breast cancer clinic, to complete a questionnaire on intentions to conceive and pregnancy outcome.
Results
A total of 175 women completed the questionnaire at a median time of 6 years from time of diagnosis. Their median age at the time of diagnosis was 37 years and at the time of the survey was 43 years. At the time of the survey, 42% (72/175) had completed their family, 41% (72/175) reported that they would like to have children and 4% (7/175) did not wish to have children. Twenty-seven respondents had actively tried to conceive, and of those 13 (48%) had a live birth. There were 12 unintended pregnancies; the majority of which were terminated (58% (7/12)) with only 3 live births. Among those who did not wish to conceive, only 32% (36/111) reported using contraception.
Conclusion
This is a retrospective study investigating menstrual function, contraceptive methods and fertility outcomes of young breast cancer survivors. This study highlights the need for healthcare professionals to provide long-term contraceptive advice to women who do not wish to conceive.

*Title Page

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Abstract

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This is a retrospective study investigating menstrual function, contraceptive methods and fertility outcomes of young breast cancer survivors. This study highlights the need for healthcare professionals to provide long-term contraceptive advice to women who do not wish to conceive.

Keywords: unplanned pregnancies, breast cancer survivors, contraception, pregnancy rate

*Revision Note

Dear Reviewers,

Thank you very much for your valuable comments. Please see below our replies to your queries and suggestions.

Reviewer #1: The present paper entitled "Planned and unplanned pregnancies in breast cancer survivors" is a retrospective survey investigating menstrual function, use of contraceptive methods and fertility outcomes according to patients' wish in young breast cancer survivors. The following points should be addressed:

1) Being the main topic of the current study, the issue of safety of pregnancy in breast cancer survivors should be discussed more in detail. Despite the high percentage of patients wishing to have a pregnancy after breast cancer (Letourneau et al, Cancer 2012) as also shown in this study, breast cancer patients are among cancer survivors those with the lowest pregnancy rate (Peccatori et al, Ann Oncol 2013). An issue of great importance in this field is that both patients (Senkus et al, Psycho Oncol 2014) and physicians (Biglia et al, Gynecol Endocrinol 2015 & Lambertini et al, Breast 2018) remain concerned on the potential detrimental prognostic effect of pregnancy in breast cancer survivors. This is not supported by recent data showing the safety of pregnancy after prior history of breast cancer (Hartman et al, Breast Cancer Res Treat 2016 & Iqbal et al, JAMA Oncol 2017 & Lambertini et al, J Natl Cancer Inst 2018 & Lambertini et al, Cancer 2019). In addition, a trial (POSITIVE study) is currently investigating the safety of interrupting endocrine therapy for allowing patients to have a pregnancy (Pagani et al, Breast 2015). This important point needs to be stressed more in depth.

Thank you very much for your very valuable and important comments. We have added these points in the main manuscript.

2) Response rate is not reported. How many patients were surveyed?

Since the questionnaire was handed in in the waiting room before their follow up appointment, all patients returned the questionnaires.

3) In both the text (including abstract) and table 2, not only absolute numbers but also percentages should be reported for the sake of clarity. Since the denominator varies in the different analysis, reporting both absolute numbers and percentages could help the readers to have a quicker understanding of the data.

Thank you very much for this suggestion. We have added as requested.

4) Some missing references that could be included are: -Epidemiology of cancer in young adult women: Fidler et al, Lancet Oncol 2017; -Gonadotoxicity of anticancer therapies in breast cancer patients: Lambertini et al, Current Opin Oncol 2018 & Codacci-Pisanelli et al, Crit Rev Oncol Hematol 2017.

-Suboptimal use of contraception in breast cancer survivors: Villareal-Garza et al, J Global Oncol 2018. –

Instead of current reference 16, the most updated guidelines on this topic should be cited: Peccatori et al, Breast 2013 & Paluch-Shimon et al, Breast 2017 & Oktay et al, J Clin Oncol 2018.

All above-mentioned references are added

5) The graphical quality of both figures is poor; they should be improved for example by using colors and clearer text. In figure 2, the use of percentages and not only absolute numbers could be helpful.
We are sorry, our original file has very clear font and colours, but it seems that there is a technical error that might have occurred during conversion into pdf format.
We will try again to upload the images.
We have added percentage in figure 2.

6) The abstract should be divided into the usual 4 sections (background, methods, results and conclusions) for the sake of clarity.
Thank you, amendments are done.

Reviewer #2: The authors present the results of survey of breast cancer survivors, exploring fertility issues in women in their early 40's. The manuscript is well written and concise. It provides an interesting insight into return of menses and fertility in these women. Before publication, I would recommend that the following issues be addressed:

-can you provide information about whether the unintentional pregnancies occurred in women taking tamoxifen/ endocrine therapy? The tamoxifen group is particularly at risk of pregnancy and may be advised to have termination if they become pregnant. This issue of tamoxifen and pregnancy planning and the challenge of whether to take women off therapy to conceive should be mentioned. Balance between declining fertility and cancer treatment.

Thank you for your question. None of the patients who had termination were on endocrine therapy.

-add % to Table 2
Thank you, we have done it
-Table 3 doesn't enhance the paper; very generic table re contraception; suggest authors consider whether it should be kept.
Thank you very much for your advice, but we still feel that this table is useful for the audience of this journal since it includes the team who is looking after breast cancer patient. And even though we would not anticipate oncologist, surgeons or breast nurses to prescribe contraception, but it would be important if this team is aware of the methods and could prompt their patient to seek advice appropriately form GP or family planning clinics.

-Please acknowledge the important role of the GP in cancer survivorship and contraception counselling; it could be argued that a GP could be more helpful than a gynaecologist for these patients.

Thank you, we have added about the role of GPs in our manuscript. However, we still believe that the main message here is for the cancer team to remind patients about importance of contraception, since GP may not necessary have direct interaction with these patients to have opportunity to discuss or advice on this matter. And certainly the role of gynaecologists here would be the least, since they are least likely to have interactions with breast cancer patients, unless patients were referred to them.

-Statistical methods description- add description of p-value calculations.
Thank you. We have added description
-you talk about hormonal contraception then about LNG-IUS as if they are different; LNG-IUS is a form of hormonal contraception; did you mean oral contraceptives in the first comment?
We have made modifications, thank you.

Highlights:

- At least 40% of women diagnosed wit breast cancer under the age of 43 still desire to conceive after completing cancer treatment
- Large proportion of women who did not use contraception in spite of having regular periods and reporting no intention to conceive
- This study established an unexpected high proportion of unintended pregnancies, 58% of which required terminated
- Its imperative for healthcare professionals to provide patients with advice not only on fertility but also contraception during and after chemotherapy

Introduction

Breast cancer is the most common cancer of women in the UK, with 1 in 8 developing this disease in their lifetime [1,2]. Approximately 23% of in situ cases and 19% of invasive breast cancer cases are diagnosed in premenopausal women [3].

Despite the increasing incidence, as a result of improved screening programmes and advances in treatment, more than 81% of women with early breast cancer survive more than ten years [4]. Current family planning trends show that women are delaying pregnancies until their late 30-40s [5], which is demonstrated by the rate of live births to mothers aged 35 and over in UK rising from 8.7% in 1990 to 20% in 2012 [6]. Similar trends are demonstrated throughout the USA [7] and the rest of the world [8]. Hence an increasing proportion of women diagnosed with breast cancer now have not attempted to conceive at the time of their diagnosis.

Despite high rates of women wishing to achieve pregnancy after breast cancer, up to 47% in some cases [9], breast cancer survivors are amongst cancer survivors with the lowest pregnancy rates [10], and 70% lower than the general population [11]. It is thought this is secondary to a number of factors including: the frequent use of gonadotoxic chemotherapy which can cause permanent amenorrhoea with complete loss of germ cells, transient amenorrhoea, menstrual irregularity and subfertility [12]. The degree of damage depends on the type of agent, patient age, original ovarian reserve, dose and duration of treatment [13]. Pregnancy is strongly discouraged during chemotherapy and radiotherapy as there is a higher risk of congenital malformations and spontaneous abortion [14].

In addition to receiving gonadotoxic treatment which can reduce the future conception rate, women are advised to avoid becoming pregnant for at least 18 months to two years when the risk of recurrence is at its highest. Patients often have prolonged treatment periods with tamoxifen in endocrine-sensitive disease and current practice is to advise against pregnancy in this period [10]. Finally, patients [15], as well as physicians [16][17], appear to remain concerned that pregnancy could simulate cancer recurrence. Recent studies contradict this hypothe-

sis [18]. Conversely, pregnancy has been hypothesized as a protective factor against breast cancer [19,20, 21]. Iqbal [19] et al found that the 5 year survival rate amongst women who became pregnant 6 month or more after their breast cancer diagnosis was 96.7% compared with 87.5% for women with no pregnancy. The POSITIVE study is currently investigating the safety of interrupting endocrine therapy to allow patients to attempt to conceive [22].

Although there are data on successful pregnancies after breast cancer, and that childbirth after diagnosis and treatment of early breast outcome does not affect outcome, there are only a few studies in the literature which look at fertility intent. Moreover, to the best of our knowledge none have followed up these women for longer than 10 years.

The aim of our study was to assess fertility outcome in relation to intent in women who had a diagnosis of early breast cancer during reproductive age.

Methods

Between August 2011 and October 2013, female cancer survivors who were diagnosed with early breast cancer up to 42 years of age (inclusive) were approached with a questionnaire during their follow-up visit to the breast clinic at Guy's and St Thomas NHS Foundation Trust.

The questionnaire (Appendix 1) was constructed by a multi-disciplinary team involving medical oncologists, a nurse consultant in breast cancer and a reproductive medicine gynecologist. The questionnaire contained 19 questions covering different aspects of menstrual and reproductive history at the time of diagnosis, and then at the time of the questionnaire: menstrual cycle history, ongoing use of contraception, subsequent pregnancies and their outcomes. In addition, we asked if the patient had completed their family, or wished to have further children in those who had children, or who wanted children or were actively trying to conceive if they had been childless prior to diagnosis. We also explored if patients were told about the potential effect of their cancer treatment on fertility, if they felt they were provided with sufficient information, and if fertility preservation was offered.

This service evaluation was approved by the Guy's and St Thomas' Foundation Trust Audit Committee. Verbal informed consent was obtained from each patient.

Statistical analysis

All data were coded and checked for errors. Missing and ambiguous responses were excluded from analysis. Descriptive statistics (i.e. frequency distribution, mean [standard deviation (SD)], and median [range]) were used to summarise characteristics and outcome variables. Differences between continuous and categorical variables were tested using T-test and the χ^2 test respectively. For all analyses, $p < 0.05$ was considered statistically significant.

Results

Characteristics of responders

We collected questionnaires from 175 patients. The primary diagnosis of breast cancer for these women was made between 1995 and 2012. The details of the responders are given in Table 1. The response rate was 100% as everyone who was approached in the clinic agreed to fill in a questionnaire, however, not all the responders answered all questions therefore absolute numbers and figures have been given to aid analysis of the results. The median age at diagnosis was 37 (25 to 42) years. At the time of this survey the median follow-up from diagnosis was 6 (1 to 21) years. The median age at the time of the survey was 43 (30-55) years. As many as 75% (131/175) of the women had chemotherapy as part of their breast cancer treatment and 33% (55/163) were still undergoing anti-breast cancer hormone treatment at the time of the survey (Table 1).

Fertility history at diagnosis

Prior to the diagnosis of breast cancer, 65% (113/175) of the responders stated they had been pregnant resulting in a live birth in 50% (87/175). In our cohort, the average reported age of conception prior to cancer diagnosis was 25 years.

Menstrual function before and after breast cancer treatment

Most women, 90% (158/175), were having periods at the time of breast cancer diagnosis; four patients were peripartum 2% (4/175). Of the patients who had adjuvant chemotherapy, 56% (74/131) reported that their periods had restarted after chemotherapy (Table 1). 21% (28/131) of patients in this cohort reported no periods after chemotherapy. As expected there was a significant difference ($P<0.0001$) in age at the time of diagnosis between patients who recovered their menstrual function after chemotherapy (35.9±4.4 years) and those who did not (39.4±2.2 years).

Contraception after treatment

Women were asked about current contraceptive use and their intention to conceive (Table 2). 64% (74/116) reported they were not using any form of contraception at the time of the survey despite not wanting to conceive. Of those not using contraception 46% (53/116) reported having their last period within last month. The median age of women not using contraception was 44 (34 to 55 years), with 85% (99/116) being under 50 years.

Desire to conceive and pregnancies after diagnosis

At the time of the survey, 42% (74/175) of women had completed their family; 4% (7/175) did not want children. 41% (72/175) wanted to have/or had more children. 20 women did not answer this question. 74% (120/164; 11 did not answer) of women stated they had a discussion with a clinician about their fertility. Of 175 responders, 14 had their embryos/eggs frozen.

Following the diagnosis, at the time of questionnaire, 26 women reported achieving a pregnancy with 16 of them resulting in a live birth (Figure 1). Not all conceptions were intentional. Among 27 women who had been trying to conceive, 13 had live births (two women were also pregnant at the time of the survey and six women had had a previous miscarriage*, with none of the patients having termination of pregnancy). Conversely, among 12 women who became pregnant unintentionally,

* some miscarriages and live birth were reported by the same patients

there were seven terminations, two miscarriages and only three live births. None of the patients who had termination were receiving tamoxifen or any other endocrine therapy.

Discussion

To the best of our knowledge this is one of the first studies assessing fertility outcome in relation to patients' intent. This study demonstrates that as many as 41% (72/175) of patients wanted to have children or more children after cancer treatment. However, only 37% (27/72) of those who wanted children have attempted to conceive so far, and of these almost half of them 48% (13/27) have been successful with a live birth.

Conversely, there was a high rate of pregnancy termination in patients who conceived unintentionally. Unexpectedly, a large proportion of patients who reported not using any contraception at the time of the survey, have also acknowledged that they did not want a child or more children.

The particular strength of this study is the length of follow-up of these women at a median of 6 years and up to 21 years. Moreover, 75% (131/175) of the women in our study had chemotherapy as part of their breast cancer treatment and 33% (55/163) were still receiving anti-breast cancer endocrine treatment at the time of the survey. This highlights the need for ongoing discussions with younger patients regarding fertility.

The retrospective nature of our study means that pregnancy age trends in our study may not be representative of trends in 2019. In our cohort the average age of having children was 25.8 years old, which is younger in comparison to the current average of 30.3 years [22]. In our study, 41% (72/175) of the women wanted a baby after breast cancer diagnosis. Due to the increasing trend of delaying pregnancy, a higher rate of women without children at breast cancer diagnosis is to be expected. Therefore, the rate of women wishing to retain fertility at breast cancer diagnosis may now be higher. Furthermore, with the increasing input from Assisted Conception Units over the last 10

to 15 years the pregnancy rate after breast cancer is likely to be higher. Only 14 women had embryo preservation in our cohort. At the time of questionnaire none of these patients had used their stored embryos.

A recent systematic review quotes pregnancy rates following breast cancer to be 3-14% [24]. The pregnancy rate after breast cancer in our study was much higher at 52% (14/27) but this is likely to be because our assessment was based on intention to conceive and the long follow-up, whereas the above-mentioned meta-analysis quoted the pregnancy rate in relation to a total number of patients who had breast cancer without adjusting for patients' intention to conceive.

Our study also raises a concern about the rate of unintended pregnancies in this population of patients. Pregnancy during breast cancer treatment should be avoided; not only can cancer treatment be teratogenic to the unborn child but also the emotional distress and difficult decision-making can have adverse psychological consequences for the women involved. A recent meta-analysis of 16 studies showed that 21% of women with a diagnosis of breast cancer terminated their subsequent pregnancies [25].

Contraceptive counselling is important, however little research has been done to establish whether patients take contraception to avoid pregnancies during this time and what advice should be given. Moreover, there is little data on unplanned pregnancies and their outcome. A large Australian population-based study showed that 47% of pregnancies that occurred 2 years following a breast cancer diagnosis were terminated [26], and that the rate of abortion was inversely proportional to the length of time between breast cancer diagnosis and subsequent pregnancy. However, authors could only speculate about the reasons behind this trend, one of which was failure of contraception.

Multiple studies have emphasised the importance of fertility counselling, but few have investigated contraceptive counselling in these women [13,26]. A retrospective Swiss study of 100 patients during their first year after breast cancer diagnosis found that circumstances leading to two unintended

pregnancies in their cohort included ineffective contraceptive methods, poor communication, and misinterpreting treatment-related amenorrhoea for the menopause [26]. Another cohort study of 104 breast cancer women in Mexico also reported poor counselling and low use of appropriate contraception during chemotherapy [27].

In our study, we found that 66% (116/175) of women at the time of the survey were not using any contraception. More surprisingly, 64% (74/116) of the women who did not use contraception did not intend to conceive, despite 42 % (31 out of 74) of them reporting having periods. Clinicians have improved counselling young breast cancer patients about fertility preservation [28, 29, 30], but a recent study showed that although oncologists felt the issue of contraception was an important aspect of discussion in breast cancer surveillance, only 30% of respondents said that they actively enquired about use of contraception [31]. Hormonal contraception, in the form of oral contraception or levonorgestrel intrauterine system (LNG- IUS), are relatively contraindicated in women with breast cancer, particularly those with oestrogen receptor positive cancer, and it is usually discontinued. Women may not want to start a new form of contraception whilst undergoing such major changes in their lives, therefore clinicians need to explain to patients the importance of contraception during breast cancer treatment and then plan for long-term contraception after definitive treatment, particularly in those women who have completed their family or do not wish to conceive. Oncologists are not necessarily experts on long-term methods of contraception and women may benefit from referral to gynaecologists. Moreover, better education should be given to general practitioners on contraceptive methods after malignancy as they are the first port of call for the patient for long-term or ongoing contraceptive advice. The current guideline of Faculty of Sexual and Reproductive Health on contraceptive choices after treatment of breast cancer recommends non-hormonal methods [32].

Use of Levonorgestrel Intrauterine System (LNG-IUS) is not usually recommended during breast cancer treatment, but can be used post breast cancer treatment with specialist advice sought if other more appropriate methods are not available or not acceptable. Table 3 outlines the different meth-

ods of contraception and their pros and cons, this is adapted from the Faculty of Sexual and Reproductive Healthcare guidelines.

The limitation of our study was that this was a retrospective questionnaire relying on women to recall facts from sometimes many years ago, and was therefore subject to recall and self-reporting bias. Although the data was collected from a large tertiary unit with a diverse population, the cohort was still limited to those patients living in the South East of England.

This study has highlighted the importance of ongoing fertility counselling in those women who wish to conceive, and in particular contraceptive counselling in those who do not. We must adopt an approach of having frank discussions with our patients at the time of diagnosis, and on follow-up, so we are able to tailor their treatment to encompass issues of fertility and prevent unintended pregnancies.

Specific questions and information regarding fertility and contraception should be part of the routine follow-up care and information offered to all patients of reproductive age following treatment for breast cancer.

Disclosure: The authors have declared no conflicts of interest

References

1. National Cancer Institute. Cancer stat facts: Female breast cancer [2018] [online] Available: https://seer.cancer.gov/statfacts/html/breast.html [April 2018]
2. Fidler MM, Gupta S, Soerjomataram I, Ferlay J, Steliarova-Foucher E, Bray F. Cancer incidence and mortality among young adults aged 20-39 years worldwide in 2012: a population-based study. Lancet Oncol. 2017;18(12):1579-1589.

3. American Cancer Society 2017. Breast cancer facts and figures [2017] [online] Available: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/breast-cancer-facts-and-figures-2017-2018.pdf

4. Office of National Health Statistics. Breast cancer statistics [2015] [online] Available: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/adhocs/004918breastcancerstatistics

5. Hayat MJ, Howlader N, Reichman ME et al. Cancer Statistics, trends, and multiple primary cancer analyses from the Surveillance, Epidemiology, and End Result Program. Oncologist 2007; 1: 20-37

6. Kenny LC, Lavender T, McNamee R et al. Advanced maternal age and adverse pregnancy outcome: evidence from a large contemporary cohort. PLoS One 2013; 8 (2): e56583. doi 10.1371/journal.pone.0056583.

7. Mathews TJ, Hamilton BE. Mean age of mothers is on the rise: United States, 2000-2014. NCHS Data Brief 2016; (232): 1-8

8. OECD Family Database. Age of mothers at childbirth and age-specific fertility [2017] [online] Available: http://www.oecd.org/els/soc/SF_2_3_Age_mothers_childbirth.pdf

9. Narod SA, Iqbal J, Giannakeas V et al. Breast cancer mortality after a diagnosis of ductal carcinoma in situ. JAMA Oncol. 2015;1(7): 888–96

10. Peccatori FA[1], Azim HA Jr, Orecchia R, Hoekstra HJ, Pavlidis N, Kesic V, Pentheroudakis G; ESMO Guidelines Working Group. Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013; 24:160-70.

11. Stensheim H, Cvancarova M, Møller B, Fosså SD. Pregnancy after adolescent and adult cancer: a population-based matched cohort study. Int J Cancer 2011; 129: 1225–1236.

~~10.~~12. Blumenfeld Z, von Wolff M. GnRH-analogues and oral contraceptives for fertility preservation in women during chemotherapy. Hum Reprod Update 2008;14: 543-552

~~11.~~13. Sonmezer M, Oktay K. Fertility preservation in young women undergoing breast cancer therapy. Oncologist 2006; 11: 422–434

~~12.~~14. Vandenbroucke T, Verheecke M, Van Calsteren K et al. Fetal outcome after prenatal exposure to chemotherapy and mechanisms of teratogenicity compared to alcohol and smoking. Expert Opin Drug Saf. 2014;13:1653–65.

~~13.~~15. Senkus E, Gomez H, Dirix L, Jerusalem G, Murray E, Van Tienhoven G, Westenberg AH, Bottomley A, Rapion J, Bogaerts J, Di Leo A, Nešković-Konstantinović Z. Attitudes of young patients with breast cancer toward fertility loss related to adjuvant systemic therapies. EORTC study 10002 BIG 3-98. Psychooncology. 2014; 23(2):173-82.

~~14.~~16. Biglia N, Torrisi R, D'Alonzo M, Codacci Pisanelli G, Rota S, Peccatori FA. Attitudes on fertility issues in breast cancer patients: an Italian survey. Gynecol Endocrinol. 2015; 31(6):458-64.

~~15.~~17. Lambertini M, Di Maio M, Pagani O, Curigliano G, Poggio F, Del Mastro L, Paluch-Shimon S, Loibl S, Partridge AH, Demeestere I, Azim HA Jr, Peccatori FA. The BCY3/BCC 2017 survey on physicians' knowledge, attitudes and practice towards fertility and pregnancy-related issues in young breast cancer patients. Breast. 2018; 42:41-49.

~~16.~~18. Hartman EK, Eslick GD. The prognosis of women diagnosed with breast cancer before, during and after pregnancy: a meta-analysis. Breast Cancer Res Treat. 2016; 160(2):347-360.

~~17.~~19. Iqbal J, Amir E, Rochon PA, Giannakeas V, Sun P, Narod SA. Association of the Timing of Pregnancy With Survival in Women With Breast Cancer. JAMA Oncol. 2017; 3(5):659-665.

~~18.~~20. Lambertini M, Kroman N, Ameye L, Cordoba O, Pinto A, Benedetti G, Jensen MB, Gelber S, Del Grande M, Ignatiadis M, de Azambuja E, Paesmans M, Peccatori FA, Azim HA Jr. Long-term Safety of Pregnancy Following Breast Cancer According to Estrogen Receptor Status. J Natl Cancer Inst. 2018; 110(4):426-429.

~~19.~~21. Lambertini M, Martel S, Campbell C, Guillaume S, Hilbers FS, Schuehly U, Korde L, Azim HA Jr, Di Cosimo S, Tenglin RC, Huober J, Baselga J, Moreno-Aspitia A, Piccart-Gebhart M, Gelber RD, de Azambuja E, Ignatiadis M. Pregnancies during and after trastuzumab and/or lapatinib in patients with human epidermal growth factor receptor 2-positive early breast cancer: Analysis from the NeoALTTO (BIG 1-06) and ALTTO (BIG 2-06) trials. Cancer. 2019; 125(2):307-316.

~~20.~~22. Pagani O, Ruggeri M, Manunta S, Saunders C, Peccatori F, Cardoso F, Kaufman B, Paluch-Shimon S, Gewefel H, Gallerani E, Abulkhair OM, Pistilli B, Warner E, Saloustros W, Perey L, Zaman K, Rabaglio M, Gelber S, Gelber RD, Goldhirsch A, Korde L, Azim HA Jr, Partridge AH. Pregnancy after breast cancer: are young patients willing to participate in clinical studies? Breast. 2015; 24(3):201–207.

~~21.~~23. Office of National Statistics. Births by parents' characteristics in England and Wales: 2016 [2017][online] Available: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/bulletins/birthsbyparentscharacteristicsinenglandandwales/2016

~~22.~~24. Gerstl B, Sullivan E, Ives A et al. Pregnancy Outcomes After a Breast Cancer Diagnosis: A Systematic Review and Meta-analysis. Clin Breast Cancer 2018; 18 e79-88

~~23.~~25. Ives A, Saunders C, Bulsara M, Semmens J. Pregnancy after breast cancer: population based study. BMJ. 2007;334(7586):194.

26. Güth U, Huang DJ, Bitzer J et al. Unintended pregnancy during the first year after breast cancer diagnosis. Eur J Contracept Reprod Health Care. 2016 Aug;21(4):290-4.

27. Castro-Sanchez A, Martinez-Cannon BA, Platas A, Mohar A, Fonseca A, Vega Y, Fimbres-Morales A, Villarreal-Garza C Suboptimal Use of Effective Contraceptive Methods in Young Mexican Women With Breast Cancer. J Glob Oncol. 2018 Oct;4:1-7.

~~24.~~28. Lee S, Schover L, Partridge A et al American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. J Clin Oncol 2006; 20: 2917–1931

29. Paluch-Shimon S, Pagani O, Partridge AH, Abulkhair O, Cardoso MJ, Dent RA, Gelmon K, Gentilini O, Harbeck N, Margulies A, Meirow D, Pruneri G, Senkus E, Spanic T, Sutliff M, Travado L, Peccatori F, Cardoso F. ESO-ESMO 3rd international consensus guidelines for breast cancer in young women (BCY3). Breast. 2017; 35:203–217.

30. Oktay K, Harvey BE, Partridge AH, Quinn GP, Reinecke J, Taylor HS, Wallace WH, Wang ET, Loren AW Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update. J Clin Oncol. 2018 Jul 1;36(19):1994-2001.

~~25.~~31. Güth I, Huang DJ, Bitzer J et al. Contraception counseling for young breast cancer patients: A practical needs assessment and a survey among medical oncologists. Breast. 2016;30:217–221

32. Faculty of Sexual and Reproductive Healthcare. UK medical eligibly criteria for contraceptive use UKMEC2016. [2016][Online] Available:https://www.fsrh.org/documents/ukmec-2016/fsrh-ukmec-full-book-2017.pdf

Introduction

Breast cancer is the most common cancer of women in the UK, with 1 in 8 developing this disease in their lifetime [1,2]. Approximately 23% of in situ cases and 19% of invasive breast cancer cases are diagnosed in premenopausal women [3].

Despite the increasing incidence, as a result of improved screening programmes and advances in treatment, more than 81% of women with early breast cancer survive more than ten years [4]. Current family planning trends show that women are delaying pregnancies until their late 30-40s [5], which is demonstrated by the rate of live births to mothers aged 35 and over in UK rising from 8.7% in 1990 to 20% in 2012 [6]. Similar trends are demonstrated throughout the USA [7] and the rest of the world [8]. Hence an increasing proportion of women diagnosed with breast cancer now have not attempted to conceive at the time of their diagnosis.

Despite high rates of women wishing to achieve pregnancy after breast cancer, up to 47% in some cases [9], breast cancer survivors are amongst cancer survivors with the lowest pregnancy rates [10], and 70% lower than the general population [11]. It is thought this is secondary to a number of factors including: the frequent use of gonadotoxic chemotherapy which can cause permanent amenorrhoea with complete loss of germ cells, transient amenorrhoea, menstrual irregularity and subfertility [12]. The degree of damage depends on the type of agent, patient age, original ovarian reserve, dose and duration of treatment [13]. Pregnancy is strongly discouraged during chemotherapy and radiotherapy as there is a higher risk of congenital malformations and spontaneous abortion [14].

In addition to receiving gonadotoxic treatment which can reduce the future conception rate, women are advised to avoid becoming pregnant for at least 18 months to two years when the risk of recurrence is at its highest. Patients often have prolonged treatment periods with tamoxifen in endocrine-sensitive disease and current practice is to advise against pregnancy in this period [10]. Finally, patients [15], as well as physicians [16][17], appear to remain concerned that pregnancy could simulate cancer recurrence. Recent studies contradict this hypothe-

sis [18]. Conversely, pregnancy has been hypothesized as a protective factor against breast cancer [19,20, 21]. Iqbal [19] et al found that the 5 year survival rate amongst women who became pregnant 6 month or more after their breast cancer diagnosis was 96.7% compared with 87.5% for women with no pregnancy. The POSITIVE study is currently investigating the safety of interrupting endocrine therapy to allow patients to attempt to conceive [22].

Although there are data on successful pregnancies after breast cancer, and that childbirth after diagnosis and treatment of early breast outcome does not affect outcome, there are only a few studies in the literature which look at fertility intent. Moreover, to the best of our knowledge none have followed up these women for longer than 10 years.

The aim of our study was to assess fertility outcome in relation to intent in women who had a diagnosis of early breast cancer during reproductive age.

Methods

Between August 2011 and October 2013, female cancer survivors who were diagnosed with early breast cancer up to 42 years of age (inclusive) were approached with a questionnaire during their follow-up visit to the breast clinic at Guy's and St Thomas NHS Foundation Trust.

The questionnaire (Appendix 1) was constructed by a multi-disciplinary team involving medical oncologists, a nurse consultant in breast cancer and a reproductive medicine gynecologist. The questionnaire contained 19 questions covering different aspects of menstrual and reproductive history at the time of diagnosis, and then at the time of the questionnaire: menstrual cycle history, ongoing use of contraception, subsequent pregnancies and their outcomes. In addition, we asked if the patient had completed their family, or wished to have further children in those who had children, or who wanted children or were actively trying to conceive if they had been childless prior to diagnosis. We also explored if patients were told about the potential effect of their cancer treatment on fertility, if they felt they were provided with sufficient information, and if fertility preservation was offered.

This service evaluation was approved by the Guy's and St Thomas' Foundation Trust Audit Committee. Verbal informed consent was obtained from each patient.

Statistical analysis

All data were coded and checked for errors. Missing and ambiguous responses were excluded from analysis. Descriptive statistics (i.e. frequency distribution, mean [standard deviation (SD)], and median [range]) were used to summarise characteristics and outcome variables. Differences between continuous and categorical variables were tested using T-test and the χ^2 test respectively. For all analyses, $p < 0.05$ was considered statistically significant.

Results

Characteristics of responders

We collected questionnaires from 175 patients. The primary diagnosis of breast cancer for these women was made between 1995 and 2012. The details of the responders are given in Table 1. The response rate was 100% as everyone who was approached in the clinic agreed to fill in a questionnaire, however, not all the responders answered all questions therefore absolute numbers and figures have been given to aid analysis of the results. The median age at diagnosis was 37 (25 to 42) years. At the time of this survey the median follow-up from diagnosis was 6 (1 to 21) years. The median age at the time of the survey was 43 (30-55) years. As many as 75% (131/175) of the women had chemotherapy as part of their breast cancer treatment and 33% (55/163) were still undergoing anti-breast cancer hormone treatment at the time of the survey (Table 1).

Fertility history at diagnosis

Prior to the diagnosis of breast cancer, 65% (113/175) of the responders stated they had been pregnant resulting in a live birth in 50% (87/175). In our cohort, the average reported age of conception prior to cancer diagnosis was 25 years.

Menstrual function before and after breast cancer treatment

Most women, 90% (158/175), were having periods at the time of breast cancer diagnosis; four patients were peripartum 2% (4/175). Of the patients who had adjuvant chemotherapy, 56% (74/131) reported that their periods had restarted after chemotherapy (Table 1). 21% (28/131) of patients in this cohort reported no periods after chemotherapy. As expected there was a significant difference ($P<0.0001$) in age at the time of diagnosis between patients who recovered their menstrual function after chemotherapy (35.9±4.4 years) and those who did not (39.4±2.2 years).

Contraception after treatment

Women were asked about current contraceptive use and their intention to conceive (Table 2). 64% (74/116) reported they were not using any form of contraception at the time of the survey despite not wanting to conceive. Of those not using contraception 46% (53/116) reported having their last period within last month. The median age of women not using contraception was 44 (34 to 55 years), with 85% (99/116) being under 50 years.

Desire to conceive and pregnancies after diagnosis

At the time of the survey, 42% (74/175) of women had completed their family; 4% (7/175) did not want children. 41% (72/175) wanted to have/or had more children. 20 women did not answer this question. 74% (120/164; 11 did not answer) of women stated they had a discussion with a clinician about their fertility. Of 175 responders, 14 had their embryos/eggs frozen.

Following the diagnosis, at the time of questionnaire, 26 women reported achieving a pregnancy with 16 of them resulting in a live birth (Figure 1). Not all conceptions were intentional. Among 27 women who had been trying to conceive, 13 had live births (two women were also pregnant at the time of the survey and six women had had a previous miscarriage*, with none of the patients having termination of pregnancy). Conversely, among 12 women who became pregnant unintentionally,

* some miscarriages and live birth were reported by the same patients

there were seven terminations, two miscarriages and only three live births. None of the patients who had termination were receiving tamoxifen or any other endocrine therapy.

Discussion

To the best of our knowledge this is one of the first studies assessing fertility outcome in relation to patients' intent. This study demonstrates that as many as 41% (72/175) of patients wanted to have children or more children after cancer treatment. However, only 37% (27/72) of those who wanted children have attempted to conceive so far, and of these almost half of them 48% (13/27) have been successful with a live birth.

Conversely, there was a high rate of pregnancy termination in patients who conceived unintentionally. Unexpectedly, a large proportion of patients who reported not using any contraception at the time of the survey, have also acknowledged that they did not want a child or more children.

The particular strength of this study is the length of follow-up of these women at a median of 6 years and up to 21 years. Moreover, 75% (131/175) of the women in our study had chemotherapy as part of their breast cancer treatment and 33% (55/163) were still receiving anti-breast cancer endocrine treatment at the time of the survey. This highlights the need for ongoing discussions with younger patients regarding fertility.

The retrospective nature of our study means that pregnancy age trends in our study may not be representative of trends in 2019. In our cohort the average age of having children was 25.8 years old, which is younger in comparison to the current average of 30.3 years [22]. In our study, 41% (72/175) of the women wanted a baby after breast cancer diagnosis. Due to the increasing trend of delaying pregnancy, a higher rate of women without children at breast cancer diagnosis is to be expected. Therefore, the rate of women wishing to retain fertility at breast cancer diagnosis may now be higher. Furthermore, with the increasing input from Assisted Conception Units over the last 10

to 15 years the pregnancy rate after breast cancer is likely to be higher. Only 14 women had embryo preservation in our cohort. At the time of questionnaire none of these patients had used their stored embryos.

A recent systematic review quotes pregnancy rates following breast cancer to be 3-14% [24]. The pregnancy rate after breast cancer in our study was much higher at 52% (14/27) but this is likely to be because our assessment was based on intention to conceive and the long follow-up, whereas the above-mentioned meta-analysis quoted the pregnancy rate in relation to a total number of patients who had breast cancer without adjusting for patients' intention to conceive.

Our study also raises a concern about the rate of unintended pregnancies in this population of patients. Pregnancy during breast cancer treatment should be avoided; not only can cancer treatment be teratogenic to the unborn child but also the emotional distress and difficult decision-making can have adverse psychological consequences for the women involved. A recent meta-analysis of 16 studies showed that 21% of women with a diagnosis of breast cancer terminated their subsequent pregnancies [25].

Contraceptive counselling is important, however little research has been done to establish whether patients take contraception to avoid pregnancies during this time and what advice should be given. Moreover, there is little data on unplanned pregnancies and their outcome. A large Australian population-based study showed that 47% of pregnancies that occurred 2 years following a breast cancer diagnosis were terminated [26], and that the rate of abortion was inversely proportional to the length of time between breast cancer diagnosis and subsequent pregnancy. However, authors could only speculate about the reasons behind this trend, one of which was failure of contraception.

Multiple studies have emphasised the importance of fertility counselling, but few have investigated contraceptive counselling in these women [13,26]. A retrospective Swiss study of 100 patients during their first year after breast cancer diagnosis found that circumstances leading to two unintended

pregnancies in their cohort included ineffective contraceptive methods, poor communication, and misinterpreting treatment-related amenorrhoea for the menopause [26]. Another cohort study of 104 breast cancer women in Mexico also reported poor counselling and low use of appropriate contraception during chemotherapy [27].

In our study, we found that 66% (116/175) of women at the time of the survey were not using any contraception. More surprisingly, 64% (74/116) of the women who did not use contraception did not intend to conceive, despite 42 % (31 out of 74) of them reporting having periods. Clinicians have improved counselling young breast cancer patients about fertility preservation [28, 29, 30], but a recent study showed that although oncologists felt the issue of contraception was an important aspect of discussion in breast cancer surveillance, only 30% of respondents said that they actively enquired about use of contraception [31]. Hormonal contraception, in the form of oral contraception or levonorgestrel intrauterine system (LNG- IUS), are relatively contraindicated in women with breast cancer, particularly those with oestrogen receptor positive cancer, and it is usually discontinued. Women may not want to start a new form of contraception whilst undergoing such major changes in their lives, therefore clinicians need to explain to patients the importance of contraception during breast cancer treatment and then plan for long-term contraception after definitive treatment, particularly in those women who have completed their family or do not wish to conceive. Oncologists are not necessarily experts on long-term methods of contraception and women may benefit from referral to gynaecologists. Moreover, better education should be given to general practitioners on contraceptive methods after malignancy as they are the first port of call for the patient for long-term or ongoing contraceptive advice. The current guideline of Faculty of Sexual and Reproductive Health on contraceptive choices after treatment of breast cancer recommends non-hormonal methods [32].

Use of Levonorgestrel Intrauterine System (LNG-IUS) is not usually recommended during breast cancer treatment, but can be used post breast cancer treatment with specialist advice sought if other more appropriate methods are not available or not acceptable. Table 3 outlines the different meth-

ods of contraception and their pros and cons, this is adapted from the Faculty of Sexual and Reproductive Healthcare guidelines.

The limitation of our study was that this was a retrospective questionnaire relying on women to recall facts from sometimes many years ago, and was therefore subject to recall and self-reporting bias. Although the data was collected from a large tertiary unit with a diverse population, the cohort was still limited to those patients living in the South East of England.

This study has highlighted the importance of ongoing fertility counselling in those women who wish to conceive, and in particular contraceptive counselling in those who do not. We must adopt an approach of having frank discussions with our patients at the time of diagnosis, and on follow-up, so we are able to tailor their treatment to encompass issues of fertility and prevent unintended pregnancies.

Specific questions and information regarding fertility and contraception should be part of the routine follow-up care and information offered to all patients of reproductive age following treatment for breast cancer.

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References

1. National Cancer Institute. Cancer stat facts: Female breast cancer [2018] [online] Available: https://seer.cancer.gov/statfacts/html/breast.html [April 2018]
2. Fidler MM, Gupta S, Soerjomataram I, Ferlay J, Steliarova-Foucher E, Bray F. Cancer incidence and mortality among young adults aged 20-39 years worldwide in 2012: a population-based study. Lancet Oncol. 2017;18(12):1579-1589.

3. American Cancer Society 2017. Breast cancer facts and figures [2017] [online] Available: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/breast-cancer-facts-and-figures-2017-2018.pdf
4. Office of National Health Statistics. Breast cancer statistics [2015] [online] Available: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/adhocs/004918breastcancerstatistics
5. Hayat MJ, Howlader N, Reichman ME et al. Cancer Statistics, trends, and multiple primary cancer analyses from the Surveillance, Epidemiology, and End Result Program. Oncologist 2007; 1: 20-37
6. Kenny LC, Lavender T, McNamee R et al. Advanced maternal age and adverse pregnancy outcome: evidence from a large contemporary cohort. PLoS One 2013; 8 (2): e56583. doi 10.1371/journal.pone.0056583.
7. Mathews TJ, Hamilton BE. Mean age of mothers is on the rise: United States, 2000-2014. NCHS Data Brief 2016; (232): 1-8
8. OECD Family Database. Age of mothers at childbirth and age-specific fertility [2017] [online] Available: http://www.oecd.org/els/soc/SF_2_3_Age_mothers_childbirth.pdf
9. Narod SA, Iqbal J, Giannakeas V et al. Breast cancer mortality after a diagnosis of ductal carcinoma in situ. JAMA Oncol. 2015;1(7): 888–96
10. Peccatori FA[1], Azim HA Jr, Orecchia R, Hoekstra HJ, Pavlidis N, Kesic V, Pentheroudakis G; ESMO Guidelines Working Group. Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013; 24:160-70.
11. Stensheim H, Cvancarova M, Møller B, Fosså SD. Pregnancy after adolescent and adult cancer: a population-based matched cohort study. Int J Cancer 2011; 129: 1225–1236.
12. Blumenfeld Z, von Wolff M. GnRH-analogues and oral contraceptives for fertility preservation in women during chemotherapy. Hum Reprod Update 2008;14: 543-552

13. Sonmezer M, Oktay K. Fertility preservation in young women undergoing breast cancer therapy. Oncologist 2006; 11: 422–434

14. Vandenbroucke T, Verheecke M, Van Calsteren K et al. Fetal outcome after prenatal exposure to chemotherapy and mechanisms of teratogenicity compared to alcohol and smoking. Expert Opin Drug Saf. 2014;13:1653–65.

15. Senkus E, Gomez H, Dirix L, Jerusalem G, Murray E, Van Tienhoven G, Westenberg AH, Bottomley A, Rapion J, Bogaerts J, Di Leo A, Nešković-Konstantinović Z. Attitudes of young patients with breast cancer toward fertility loss related to adjuvant systemic therapies. EORTC study 10002 BIG 3-98. Psychooncology. 2014; 23(2):173-82.

16. Biglia N, Torrisi R, D'Alonzo M, Codacci Pisanelli G, Rota S, Peccatori FA. Attitudes on fertility issues in breast cancer patients: an Italian survey. Gynecol Endocrinol. 2015; 31(6):458-64.

17. Lambertini M, Di Maio M, Pagani O, Curigliano G, Poggio F, Del Mastro L, Paluch-Shimon S, Loibl S, Partridge AH, Demeestere I, Azim HA Jr, Peccatori FA. The BCY3/BCC 2017 survey on physicians' knowledge, attitudes and practice towards fertility and pregnancy-related issues in young breast cancer patients. Breast. 2018; 42:41-49.

18. Hartman EK, Eslick GD. The prognosis of women diagnosed with breast cancer before, during and after pregnancy: a meta-analysis. Breast Cancer Res Treat. 2016; 160(2):347-360.

19. Iqbal J, Amir E, Rochon PA, Giannakeas V, Sun P, Narod SA. Association of the Timing of Pregnancy With Survival in Women With Breast Cancer. JAMA Oncol. 2017; 3(5):659-665.

20. Lambertini M, Kroman N, Ameye L, Cordoba O, Pinto A, Benedetti G, Jensen MB, Gelber S, Del Grande M, Ignatiadis M, de Azambuja E, Paesmans M, Peccatori FA, Azim HA Jr. Long-term Safety of Pregnancy Following Breast Cancer According to Estrogen Receptor Status. J Natl Cancer Inst. 2018; 110(4):426-429.

21. Lambertini M, Martel S, Campbell C, Guillaume S, Hilbers FS, Schuehly U, Korde L, Azim HA Jr, Di Cosimo S, Tenglin RC, Huober J, Baselga J, Moreno-Aspitia A, Piccart-Gebhart M, Gelber RD, de Azambuja E, Ignatiadis M. Pregnancies during and after trastuzumab and/or lapatinib in patients with human epidermal growth factor receptor 2-positive early breast cancer: Analysis from the NeoALTTO (BIG 1-06) and ALTTO (BIG 2-06) trials. Cancer. 2019; 125(2):307-316.

22. Pagani O, Ruggeri M, Manunta S, Saunders C, Peccatori F, Cardoso F, Kaufman B, Paluch-Shimon S, Gewefel H, Gallerani E, Abulkhair OM, Pistilli B, Warner E, Saloustros W, Perey L, Zaman K, Rabaglio M, Gelber S, Gelber RD, Goldhirsch A, Korde L, Azim HA Jr, Partridge AH. Pregnancy after breast cancer: are young patients willing to participate in clinical studies? Breast. 2015; 24(3):201–207.

23. Office of National Statistics. Births by parents' characteristics in England and Wales: 2016 [2017][online] Available: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/bulletins/birthsbyparentscharacteristicsinenglandandwales/2016

24. Gerstl B, Sullivan E, Ives A et al. Pregnancy Outcomes After a Breast Cancer Diagnosis: A Systematic Review and Meta-analysis. Clin Breast Cancer 2018; 18 e79-88

25. Ives A, Saunders C, Bulsara M, Semmens J. Pregnancy after breast cancer: population based study. BMJ. 2007;334(7586):194.

26. Güth U, Huang DJ, Bitzer J et al. Unintended pregnancy during the first year after breast cancer diagnosis. Eur J Contracept Reprod Health Care. 2016 Aug;21(4):290-4.

27. Castro-Sanchez A, Martinez-Cannon BA, Platas A, Mohar A, Fonseca A, Vega Y, Fimbres-Morales A, Villarreal-Garza C Suboptimal Use of Effective Contraceptive Methods in Young Mexican Women With Breast Cancer. J Glob Oncol. 2018 Oct;4:1-7.

28. Lee S, Schover L, Partridge A et al American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. J Clin Oncol 2006; 20: 2917–1931

29. Paluch-Shimon S, Pagani O, Partridge AH, Abulkhair O, Cardoso MJ, Dent RA, Gelmon K, Gentilini O, Harbeck N, Margulies A, Meirow D, Pruneri G, Senkus E, Spanic T, Sutliff M, Travado L, Peccatori F, Cardoso F. ESO-ESMO 3rd international consensus guidelines for breast cancer in young women (BCY3). Breast. 2017; 35:203–217.

30. Oktay K, Harvey BE, Partridge AH, Quinn GP, Reinecke J, Taylor HS, Wallace WH, Wang ET, Loren AW Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update. J Clin Oncol. 2018 Jul 1;36(19):1994-2001.

31. Güth I, Huang DJ, Bitzer J et al. Contraception counseling for young breast cancer patients: A practical needs assessment and a survey among medical oncologists. Breast. 2016;30:217–221

32. Faculty of Sexual and Reproductive Healthcare. UK medical eligibly criteria for contraceptive use UKMEC2016. [2016][Online] Available:https://www.fsrh.org/documents/ukmec-2016/fsrh-ukmec-full-book-2017.pdf

Table

Table 1 Characteristics of respondents

Age of patients at the time of cancer diagnosis	
Median age, years Range	37 25 to 42
Time since diagnosis	
Median, years Range	6 1 to 21
Age of patients at the time of questionnaire	
Median age, years	43
Range, years	30-55
Menstrual function at diagnosis	N=175
Had periods Peripartum No periods Not answered	158 (90%) 4 (2%) 4 (2%) 9 (5%)
Menstrual function after chemotherapy (n=131)	N=131
Periods restarted after chemo Periods did not restart after periods Periods not affected by chemo (did not stop) Not answered	74 (56%) 28 (21%) 21 (16%) 8 (6%)
Previous pregnancies before cancer diagnosis	N=175
No Yes Not answered	51(29%) 113 (65%) 11 (6%)
Previous live birth	87 (50%)
Treatment of breast cancer (reported by patients)	
Chemotherapy for treatment reported by patients	131 (75%)
Current Anti-estrogen Therapy Yes No Not answered	 57 (33%) 106 (60%) 12 (7%)

Table 2 Intention to conceive and reported contraception usage

Intention to conceive	Contraception reported	No contraception	Not answered	Total
Yes	4 (15%)	22 (81%)	1 (0.04%)	27 (15%)
No	36 (32%)	74 (67%)	1 (1%)	111 (63%)
Not answered	3 (4%)	9 (36%)	13 (52%)	25 (14%)
Not applicable	1 (8%)	11 (92%)	0	12 (7%)
Total	44 (25%)	116 (66%)	15(9%)	175

Table 3: Summary of different methods of contraception available adopted from the Faculty of Sexual and Reproductive Healthcare Guidelines https://www.fsrh.org/home/

Type of Contraception	Positives	Negatives
Condoms	Low failure rate Cheap Protects against sexually transmitted infections	Not long-acting form of contraception
Caps	Can be inserted and removed by patient themselves	Not readily available Must not be removed until 6 hours post coitus Expensive
Copper IUD	Long term form of contraception Can be used with breast cancer treatment	Can cause menorrhagia, dysmenorrhoea Invasive
LNG-IUS (levonorgestrel-intrauterine system)	Long term form of contraception Counteracts the proliferation effects of tamoxifen in endometrium Can reduce menorrhagia	Little data on use and recurrence of breast cancer. Specialist opinion should be sought before use in past history of breast cancer. Contraindicated in current breast cancer treatment
Progestrone only Implant		Contraindicated in current breast cancer treatment Specialist opinion should be sought before use in past history of breast cancer.
Depot medroxyprogesterone acetate		Contraindicated in current breast cancer treatment. Specialist opinion should be sought before use in past history of breast cancer.
Progestogen only pill		Contraindicated in current breast cancer treatment. Specialist opinion should be sought before use in past history of breast cancer.

Combined hormonal contraception		Contraindicated in current breast cancer treatment. Specialist opinion should be sought before use in past history of breast cancer.

Figure

Figure 1 Intention to conceive after cancer treatment

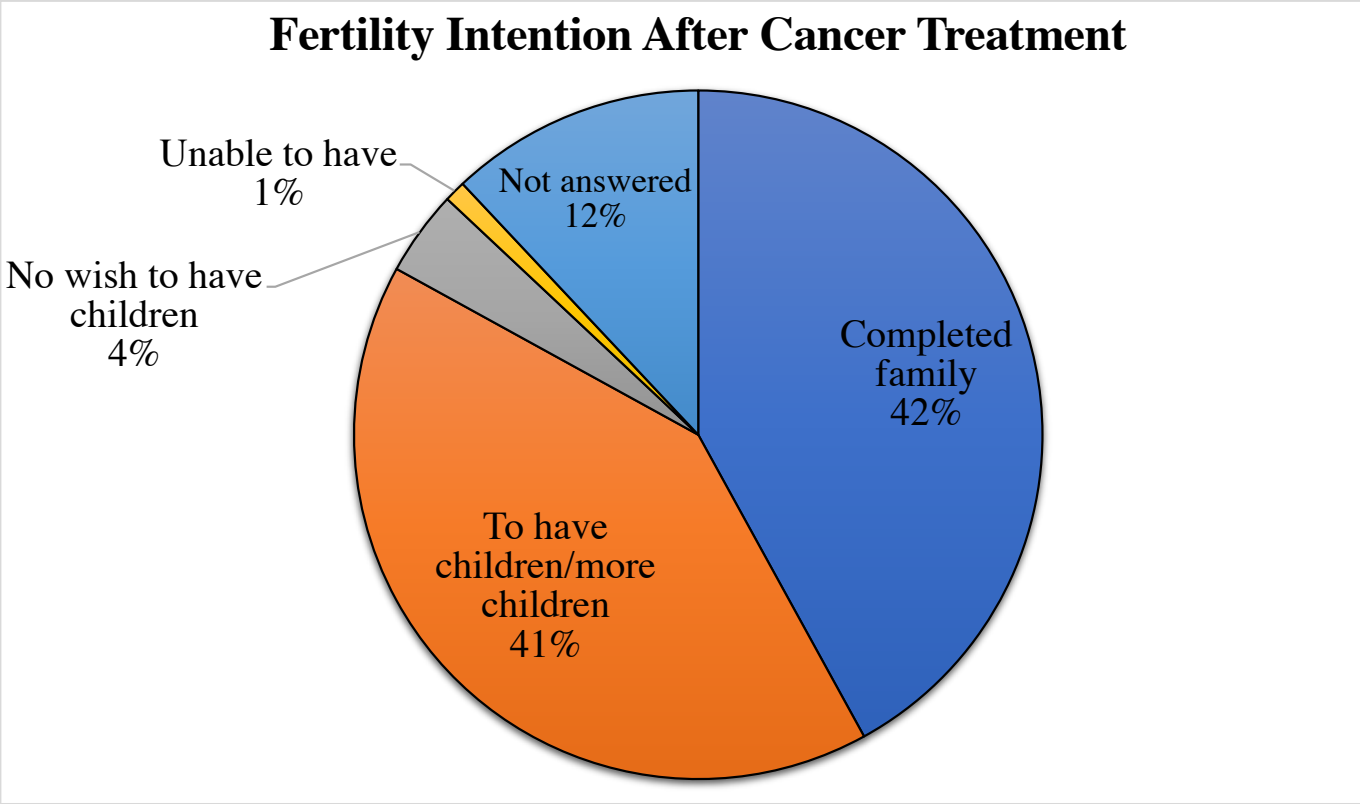
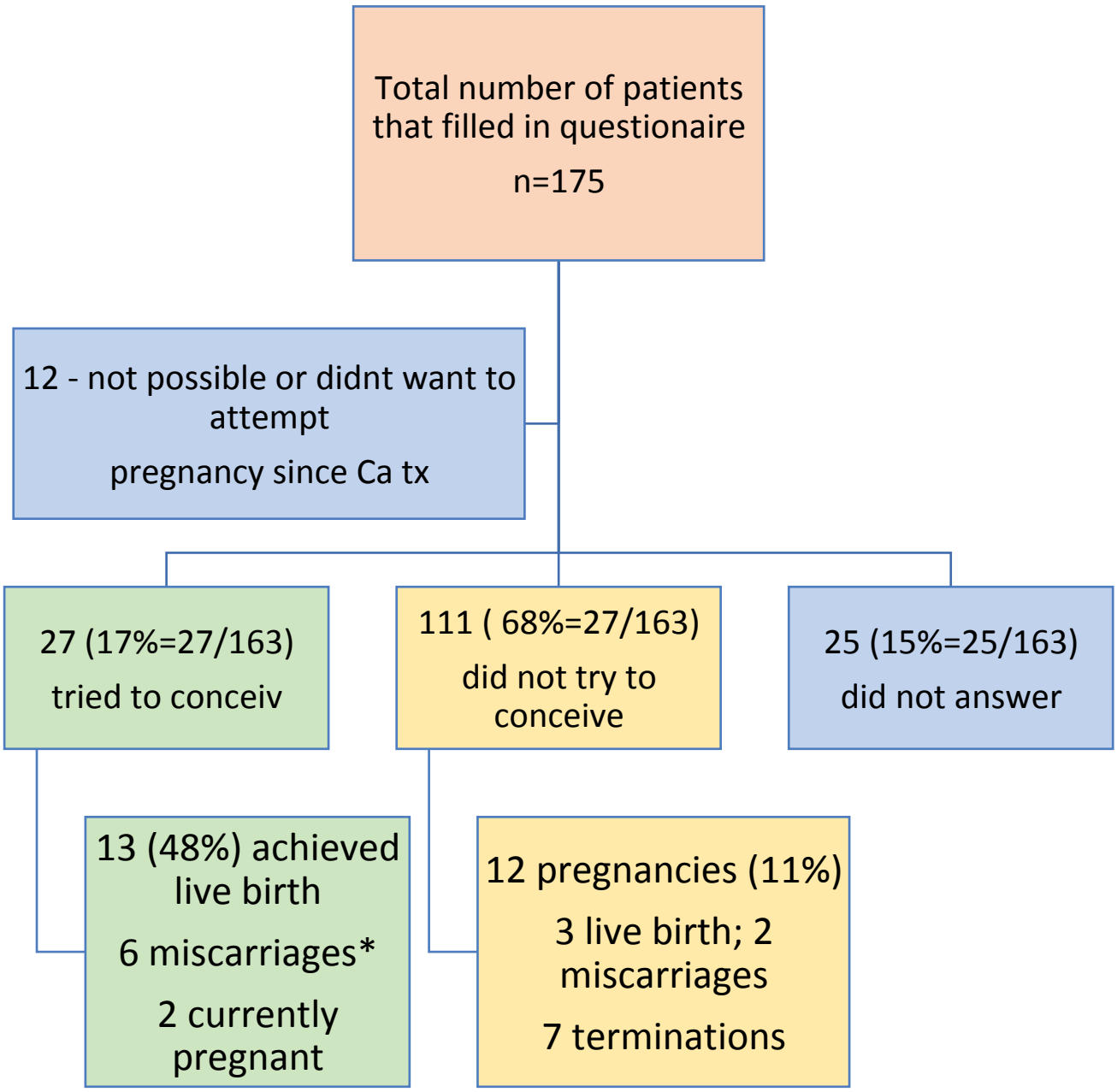


Figure 2 Pregnancy outcomes in breast cancer patients after treatment.



*Some patients had more than one pregnancy that result in miscarriage or live birth